

## STATISTICAL SHAPE ANALYSIS OF BRAIN STRUCTURES

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Quantitative morphologic assessment of brain structures is routinely based on volumetric measurements. Volume changes are intuitive features as they might explain atrophy or dilation due to illness. On the other hand, structural changes at specific locations are not sufficiently reflected in volume measurements. Shape analysis has thus become of increasing relevance to the neuroimaging community due to its potential to precisely locate morphological changes between healthy and pathological structures.

Within the NA-MIC network, the following key problems in structural shape analysis are being tackled in a joint effort: shape representation, correspondence, statistical testing, and tool development. A first, basic framework and set of tools for statistical shape analysis based on a sampled local spherical harmonic shape representation (SPHARM-PDM) has been implemented. Within this shape analysis framework further methodological developments have been developed: Representation: Two additional shape representations complement SPHARM-PDM. A novel spherical wavelet based representation allows a hierarchical decomposition and an increased sensitivity of the statistical analysis through a reduction of the number of shape features. Another novel particle-system based representation allows the analysis of structures of non-spherical topology, such as the cranium, as well as is insensitive to noise-induced topological variations. Correspondence: A new method is in development for the correspondence of surface points across different datasets using a population-wise optimization of a curvature metric. Based on our earlier comparisons studies, this method will enhance the anatomical correctness, the statistical modeling properties, as well as the statistical sensitivity.

Statistical Testing: We developed methods for the computation of group discrimination as well as non-parametric statistical hypothesis testing. Also, correction for multiple-comparison testing has been incorporated into the statistical shape analysis framework based on two complementing approaches, family-wise error control via permutation testing and false discovery rate control. These correction methods are crucial in enhancing the sensitivity and the power of the analysis. Tool Development: Based on closed interaction with the engineering core, shape analysis tools were developed within the Insight Toolkit (ITK) framework. These tools have been incorporated into the LONI pipeline software, and disseminated to several clinical collaborators within and outside the NA-MIC network.

We applied the SPHARM-PDM shape analysis tools on data from a male schizo-typal personality disorder (SPD) study (VA Brockton, BWH) available within the NA-MIC data repository. The results show significant shape differences located in the posterior and anterior parts of the caudate head on both hemispheric structures, but enhanced on the right caudate. Additional results computed using the same tools on a new female SPD study showed similar findings with enhanced sensitivity due to an enlarged sample size. Both of these datasets have also been analyzed using the spherical wavelet based representation based on the SPHARM correspondence. These results both confirmed the earlier ones, as well as extended the significance pattern in regard to a hierarchical decomposition. Current studies are in progress using the novel particle based approach, as well as using the enhanced curvature based correspondence method.